

Claims 1-10 have been cancelled without prejudice and rewritten as new claims 11-20. The new claims have been presented to put the claims in better form and to overcome the rejections under 35 USC § 101 and 112. Further, new claims 21 and 22 have been added to further protect specific embodiments of the present invention. Support for the new claims is readily apparent from the teachings of specification and the original claims.

With regard to the objection of claims 3, 6 and 7, this objection is believed to be overcome by the wording of the new claims. Specifically, the phrase “making hybrid eukaryotic species” has been omitted from corresponding new claim 13. Further, claims 6 and 7 have been rewritten as new claims 16 and 17 to specify eukaryotic homologues of the *mutS* protein and/or *mutL* protein as per the Examiner’s suggestion. Thus, in light of the new claims, Applicant respectfully request that this objection be withdrawn.

With regard to the rejection of claims 1, 2, 6 and 7 under 35 USC § 101, this rejection is deemed to be untenable in view of the wording of the new claims and is thus respectfully traversed. Specifically, the new claims have been amended to recite that the eukaryotic cells containing the partially homologous DNA sequences are genetically or physiologically manipulated to render defective the enzymatic mismatch repair system of the eukaryotic cells. This amendment clearly distinguish the present invention from naturally occurring defects of mismatch repair genes where no “manipulation” is present. Thus, in view of the new claims, Applicant respectfully submit that this rejection can no longer be sustained and should be withdrawn.

With regard to the rejection of claims 1-3, 6 and 7 under 35 USC § 112, second paragraph, Applicants believe that each ground of rejection has been overcome in view of the wording of the

new claims. Specifically, Applicants have changed the phrase “to effect meiosis” in the new claims to “to result in the meiotic recombination *in vivo* of said partially homologous DNA sequences”. This language has been added to the new claims to clearly specify that all culturing conditions which allow for meiosis to occur is encompassed by the claimed invention. This language does not differentiate between conditions which allow meiosis to occur and conditions which effect or cause meiosis. Applicant believe that “culturing conditions” which result in meiosis are well known and understood to one skilled in the art and are clearly definite under 35 USC § 112, second paragraph.

With regard to the Examiner’s rejection of the term “genes”, Applicants believe that the Examiner is mistaken in this regard. The term “genes” is a well understood term in biotechnology. It has been defined to mean “an ordered sequence of nucleotides located in a particular position on a particular chromosome that encodes a specific functional product.” Thus, it can be interpreted to include and not include noncoding sequences such as promoters and 5' and 3' untranslated regions.

With regard to the Examiner’s remaining grounds of rejection for claims 3, 6 and 7, Applicants believe the wording of the new claims specifically addresses and resolve the Examiner’s concerns.

Thus, in light of the above, Applicants believe that claims 1-3, 6 and 7 are definite under 35 USC § 112, second paragraph, and that this rejection should be withdrawn.

With regard to the rejection of claim 3 under 35 USC § 112, first paragraph, this rejection is believed to be overcome by the wording of new claim 13 and is thus respectfully traversed. Specifically, original claim 3 has been rewritten as new claim 13 to delete the phrase “making hybrid eukaryotic species”. Thus, this rejection is no longer sustainable in view of new claim 13.

With regard to the rejection of claims 1, 2, 6 and 7 under 35 USC § 102(b) as being anticipated by Thomas (Curr. Opin. Oncol., 6(4):406-412, 1994), this rejection is deemed to be untenable and is thus respectfully traversed.

To constitute anticipation of the claimed invention, a single prior art reference must disclose each and every material element of the claims. Here, in this case, it is clear that Thomas does not teach each and every material element of the claims.

The present invention involves the genetic or physiological manipulation of eukaryotic cells containing partially homologous DNA sequences to render defective the enzymatic mismatch repair system of these eukaryotic cells. It is not directed to naturally occurring meiotic recombination process in mismatch repair defective animals

Further, Applicants believe that the Examiner is not wholly correct in his opinion of the example relating to hereditary non-polyposis colorectal cancer (HNPCC), found in the paragraph bridging pages 2 and 3 of the Official Action. HNPCC patients are MSH2 heterozygotes (MSH2+/-) and are fully proficient in mismatch repair. Only when tumours become homozygotes (MSH2-/-) are they deficient in mismatch repair. The Examiner states at the end of the first paragraph on page 3, "... and yet they are reproductively fertile". This appears to be a misunderstanding. The aim of producing mutant mismatch repair deficient cells is to provide a reproductively fertile organism when the situation arises when the mismatch repair genes are of the wild type, and recombination and fertility would not be achieved i.e. during interspecies crosses (see page 2, lines 15 to 26). The disclosure of Thomas merely shows that there is an association between HNPCC and MSH2 defects. Thus, the cited document does not teach or suggest the present invention.

As a result, Applicant respectfully request that this rejection of claims 1, 2, 6 and 7 under 35 USC § 102(b) be withdrawn.

In view of the foregoing amendments and remarks, Applicants believe that the application is now in condition for allowance. Such action is thus respectfully solicited.

If, however, the Examiner has any suggestions for expediting the allowance of the application or believes that direct communication with Applicants' attorney will advance the prosecution of this case, the Examiner is invited to contact the undersigned at the telephone number below.

Respectfully submitted,

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